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EXAMINER	
SCHLAPKOHL, WALTER	
ART UNIT	**PAPER NUMBER**
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/550,173	OOE ET AL.	
	Examiner	Art Unit	
	Walter Schlapkohl	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-17 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11-17 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/9/04 and 8/14/00*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of the papers filed 1/23/2006 in which claim 19 was added. Claims 1-9, 11-17 and 19 are pending and under examination in the instant application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 1/23/2006 has been entered.

Specification

The amendment filed 4/3/2003 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The

added material which is not supported by the original disclosure is as follows:

Note: Examiner has bolded and underlined Applicant's amendments of the specification from page 3, line 26, to page 8, line 19 which, by deletion, add new matter to the specification:

> The present invention provides:
> [1.] an animal cell expressing a gene coding a ligand-responsive transcription control factor and securely maintaining a DNA comprising in a molecule, the following genes (a) and (b):
> (a) a reporter gene connected downstream from a transcription control region, in which said transcription control region substantially consists of a recognition sequence of said ligand-responsive transcription control factor and a minimum promoter which can function in said cell; and
> (b) a selective marker gene which can function in said cell; provided that the following gene (c):
> (c) a reporter gene connected downstream from a promoter which transcription activity is unchanged by having said responsive transcription control factor contacted with a ligand of said ligand-responsive transcription control factor, said reporter gene (c) coding a protein which can be differentiated from the protein coded by said gene (a) is not present in said cell;
> [2.] the cell according to the above [1], wherein said minimum promoter substantially consists of a TATA box;
> [3.] the cell according to the above **[1]**, wherein said ligand-responsive transcription control factor is one selected from an aryl hydrocarbon receptor, intranuclear hormone receptor, estrogen receptor, androgen receptor and thyroid hormone receptor;
> [4.] the cell according to the above **[1]**, wherein said ligand-responsive control factor is an aryl hydrocarbon receptor;
> [5.] the cell according to the above **[1]**, wherein said ligand-responsive control factor is an intranuclear hormone receptor;
> [6.] the cell according to the above **[1]**, wherein said ligand-responsive control factor is an estrogen receptor;

[7.] the cell according to the above **[1]**, wherein said ligand-responsive control factor is an androgen receptor;

[8.] the cell according to the above **[1]**, wherein said ligand-responsive control factor is a thyroid hormone receptor;

[9.] an animal cell expressing an aryl hydrocarbon receptor and an Arnt receptor, and securely maintaining a DNA comprising in a molecule, the following genes (a) and (b):

(a) a reporter gene connected downstream from a transcription control region, wherein said transcription control region substantially consists of a recognition sequence of said aryl hydrocarbon receptor and a minimum promoter which can function in said cell; and

(b) a selective marker gene which can function in said cell; provided that the following gene (c):

(c) a reporter gene connected downstream from a promoter which transcription activity is unchanged by having said responsive transcription control factor contacted with a ligand of said ligand-responsive transcription control factor, said reporter gene (c) coding a protein which can be differentiated from the protein coded by said gene (a) is not present in said cell;

[10.] use of an animal cell **[according to any one of the above 1 to 9]** for evaluating an agonist activity of a chemical substance over the transcription promoting ability of a ligand-responsive transcription control factor, in a reporter assay measuring the amount of a reporter gene under transcription control of said ligand-responsive transcription control factor;

[11.] a method for evaluating a chemical substance to have agonist activity over the transcription promoting ability of a ligand-responsive transcription control factor, said method comprising:

(i) culturing an animal cell **[according to any one of claims 1 to 9]** in the presence of the chemical substance;

(ii) measuring the expression amount of a reporter gene in said cell and

(iii) assessing said chemical substance to have agonist activity over the transcription promoting ability of the ligand-responsive transcription control factor when the measured value of expression amount of said reporter gene introduced into said cell is larger than a measured value of expression amount of said reporter gene in the absence of said chemical substance;

[12.] a method for evaluating a chemical substance to have antagonist activity over the transcription promoting ability of a ligand-responsive transcription control factor, said method comprising:

(i) culturing an animal cell **[according to any one of claims 1 to 9]** in the presence of the chemical substance;

(ii) measuring the expression amount of a reporter gene in said cell and

(iii) assessing said chemical substance to have agonist activity over the transcription promoting ability of the ligand-responsive transcription control factor when the measured value of expression amount of said reporter gene introduced into said cell is larger than a measured value of expression amount of said reporter gene in the absence of said chemical substance;

[13.] a measuring kit comprising an animal cell **[according to any one of the above 1 to 9];**

[14.] a method for obtaining an animal cell for measuring the activity of a ligand-responsive transcription control factor, said method comprising:

(i) introducing into an animal cell, a DNA comprising in a molecule the following genes (a) and (b):

(a) a reporter gene connected downstream from a transcription control region, wherein said transcription control region substantially consists of a recognition sequence of said ligand-responsive transcription control factor and a minimum promoter which can function in said cell; and

(b) a selective marker gene which can function in said cell,

said animal cell being

an animal cell that comprises a DNA comprising a gene coding the ligand-responsive transcription control factor introduced thereto before, after or during the same time of above step (i) or that naturally having an ability to express the gene coding the ligand-responsive transcription control factor, provided that a reporter gene (c) connected downstream from a promoter which transcription activity is unchanged by having said responsive transcription control factor, said reporter gene (c) coding a protein which can be differentiated from the protein coded by said gene (a), is not present in the cell; and (ii) recovering from the transformed cell obtained from step (i), a transformed cell having said introduced DNA securely maintained therein;

> [15.] the method according to the above **[14]**, wherein said cell is an animal cell that comprises a DNA comprising a gene coding the ligand-responsive transcription control factor introduced thereto before, after or during the same time of the step (i);
>
> [16.] the method according to the above **[15]**, wherein the DNA comprising a gene coding the ligand-responsive transcription control factor, comprises in a molecule, a selective marker gene which can function in said cell and which codes a phenotype different from that of the gene (b).

Applicant is required to cancel the new matter in the reply to this Office Action. Applicant is reminded, however, that reference to claims within the specification are not allowed as claims may be amended during the course of prosecution.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-12, 14-15 & 17, and therefore dependent claims 16 and 19, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 recites "assessing said chemical substance to have agonist activity over the transcription promoting ability of the ligand-responsive transcription control factor when the measured value of expression amount of said reporter gene (a) introduced into said cell is larger than a measured value of expression amount of said reporter gene (a) in the absence of said chemical substance" in lines 7-11. Claim 11 is vague and indefinite in that it is unclear which values of expression amount are actually being compared. Can *any* value of expression amount of reporter gene (a) in the absence of said chemical substance be used to compare to *any* value of expression amount of said reporter gene (a) in the presence of the chemical substance, or are there limitations on which values of expression amount can be compared?

Similarly, claim 12 recites "assessing said chemical substance to have antagonist activity over the transcription promoting ability of the ligand-responsive transcription control factor when the measured value of expression amount of said reporter gene (a) introduced into said cell is smaller than a measured value of expression amount of said reporter gene (a) in the presence of said ligand and the absence of said chemical substance" in lines 7-11. Can *any* value of expression amount of reporter gene (a) in the presence of said chemical substance and

said ligand be used to compare to *any* value of expression amount of said reporter gene (a) in the absence of the chemical substance, or are there limitations on which values of expression amount can be compared?

Claim 14 recites "[a] method for obtaining an animal cell for measuring the ability to control the activity of a ligand-responsive transcription control factor, said method comprising: (i) introducing into an animal cell, a DNA comprising in a molecule the following genes (a) and (b): a reporter gene connected downstream from a transcription control region wherein said transcription control region substantially consists of a recognition sequence of said ligand-responsive transcription control factor and a minimum promoter which can function in said cell, and (b) a selective marker gene which can function in said cell, said animal cell being an animal cell that comprises a DNA comprising a gene coding the ligand-responsive control factor introduced thereto before, after or during the same time of above step (i) or that naturally has an ability to express the gene coding the ligand-responsive transcription control factor" in lines 1-14. Claim 14 is vague and indefinite in that it is unclear if Applicant is referring to the step (i) of the instant claim or to step (i) of some other claim since the reference to "the above step (i)" is made within the context of step (i)

itself. Claim 14 is also vague and indefinite in that it is unclear whether the DNA comprising the ligand-responsive transcription control factor is being introduced into the cell or whether the ligand-responsive transcription control factor is being introduced into the DNA.

Similarly, claim 15 recites "[t]he method of claim 14, wherein said cell is an animal cell that comprises a DNA comprising a gene coding the ligand-responsive transcription control factor introduced thereto before, after or during the same time of the step (i)" in lines 1-3. Claim 15 is vague and indefinite in that it is unclear if the gene coding the ligand-responsive transcription control factor is being introduced to a DNA or if the DNA is being introduced to an animal cell before, after or during the same time as step (i) of claim 14.

Claim 17 recites "[a]n animal cell expressing a gene coding a ligand-responsive transcription control factor and stably transformed with a DNA comprising in a molecule, the following genes (a) and (b):

(a) a reporter gene connected downstream from a transcription control region; wherein said transcription control region contains a minimum promoter and a recognition sequence of the ligand-responsive transcription control factor and contains no sequence having the transcription control ability changed by

the ligand-responsive transcription control factor recognition sequence and minimum promoter" in lines 1-8. Claim 17 is vague and indefinite in that it is unclear what is meant by "no sequence having the transcription control ability changed by the ligand-responsive transcription control factor recognition sequence and minimum promoter." Does Applicant intend that the the presence of a minimum promoter and a recognition sequence of the ligand-responsive transcription control factor should not change the transcription control ability of the of the transcription control region, or does Applicant intend that the transcription control region does not contain any sequence which would alter the activity of a transcription control region containing a minimal promoter and a recognition sequence of a ligand-responsive transcription control factor?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 19 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

The specification as originally filed does not provide support for the invention as now claimed: "[t]he cell according to any one of claims 1, 2, 9 and 17, wherein said minimum promoter is a minimum promoter of metallothionein I gene or ovalbumin gene." The specification does not provide sufficient blazemarks nor direction for the instant minimum promoters encompassed by the above-mentioned limitation, as currently recited. The instant specification only provides sufficient blazemarks and direction for minimal promoters of the mouse metallothionein I gene and chicken ovalbumin gene. The instant claims now recite a limitation, which was not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such a limitation recited in the present claims, which did not appear in the specification as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Claims 1-9, 11-17 and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to animal cells expressing a gene coding a ligand-responsive transcription control factor (LRTF) and stably transformed with a DNA comprising in a molecule a reporter gene (a) and a selective marker gene (b). The claims encompass any animal cell expressing any gene coding an LRTF and stably transformed with a reporter gene and a selective marker gene. The claims do not provide any structural information with regard to the genes (promoters, enhancers, exon and intron sequences and boundaries, 3′ untranslated region sequences) capable of being expressed in and/or stably transformed in a molecule. Thus, the rejected claims thus comprise a set of nucleic acid sequences that are defined by the coding region of a gene.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the

genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and any combination thereof. The specification describes plasmids comprising in a molecule both an LRTF recognition sequence (e.g. from an aryl hydrocarbon receptor) and a minimum promoter (e.g. from the mouse metallothionein I gene) operatively linked to a reporter "gene" (e.g., the firefly luciferase coding region) transfected into NIH 3T3 cells or HeLa cells, but the specification does not describe the *genes* themselves, including the 5′ and 3′ elements as well the introns and exons and their corresponding sequences. No description is provided of a single animal cell comprising an entire gene sequence for an LRTF and which has been stably transformed with the entire gene sequence for a reporter gene and/or a marker gene.

Given the very large genus of nucleic acid molecules and cells encompassed by the rejected claims, and given the limited description provided by the specification with regard to the gene elements (5′ and 3′ regulator elements, intron and exon structure and sequences) capable of fulfilling the claim limitations of claims 1-9, 11-17 and 19, the skilled artisan would not have been able to describe the broadly claimed genus

of LRTF, reporter and marker *genes* that meet the claim limitations. Thus, there is no structural/functional basis provided by the prior art or instant specification for one of skill in the art to envision those nucleic acid sequences that satisfy the functional limitations of the claims. Therefore, the skilled artisan would have reasonably concluded Applicant was not in possession of the claimed invention for claims 1-9, 11-17 and 19.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 5, 13-14 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Mader and White (US Patent No. 5,512,483; henceforth Mader).

Note: where Applicant's claims have been found vague and indefinite as cited above, Applicant's invention has been interpreted for this rejection only as set forth below:

Applicant's invention includes an animal cell (claim 1) or a kit thereof (claim 13) that is stably transformed with a DNA comprising in a molecule, a reporter gene (a) connected downstream from a transcription control region, in which said transcription control region contains exclusively the intended ligand-responsive transcription control factor (LRTF) recognition sequence and a minimum promoter as the main functional element relating to transcription control, and a selectable marker (b), but does not contain a reporter gene (c) which is not responsive to said transcription response element. The claims further encompass such a cell wherein the minimum promoter is a TATA box (claim 2), wherein the LRTF is an intranuclear hormone receptor (claim 5). The claims are further drawn to such a cell wherein the transcription control region does not contain a sequence which would alter the transcription control activity as determined by the minimum promoter region and the LRTF recognition sequence (claim 17). The claims are further drawn to a method for obtaining such a cell wherein the cell is an animal cell that comprises a DNA comprising a gene coding the LRTF which was introduced thereto before, after or during the same time as the reporter gene and marker gene are introduced into the cell (claims 14), and such a cell wherein

the gene coding the LRTF comprises a selective marker gene different from gene (b) (claim 16).

Mader teaches a mammalian expression vector composed of several high affinity glucocorticoid response elements (GREs) placed upstream of a minimal promoter TATA region and which further comprises a reporter gene (CAT) and a selective marker gene (see entire document, especially paragraph bridging columns 2 and 3; and Figure 1). Mader further teaches that the vector is introduced stably into the HeLa cell genome. HeLa cells express an endogenous gene coding a ligand-responsive transcription control factor (the glucocorticoid receptor), and the cells further do not comprise a reporter gene connected downstream from a promoter which transcription activity is not changed by having said LGTF contacted with a ligand of said LGTF. Regarding claim 5, the glucocorticoid receptor is an intranuclear hormone receptor. Regarding claims 13-14 and 17, Mader teaches such an animal cell and a method of obtaining such a cell.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-9, 11 and 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bradfield et al (US Patent No. 5,650,283, of record; henceforth Bradfield) in view of Waldman and Waldman (Analytical Biochemistry 258:216-222, 1998, of record; henceforth Waldman).

This rejection is maintained for reasons of record.

Note: where Applicant's claims have been found vague and indefinite as cited above, Applicant's invention has been interpreted for this rejection only as set forth below: Applicant's invention includes an animal cell (claim 1) or a kit thereof (claim 13) that is stably transformed with a DNA comprising in a molecule, a reporter gene (a) connected downstream from a transcription control region, in which said transcription control region contains exclusively the intended ligand-responsive transcription control factor (LRTF) recognition sequence and a minimum promoter as the main functional element relating to transcription control, and a selectable marker (b), but does not contain a reporter gene (c) which is not responsive to said transcription response element. The claims further encompass such a cell wherein the minimum promoter is a TATA box (claim 2), a metallothionein I gene or an ovalbumin gene minimum promoter (claim 19), wherein the LRTF is selected from an aryl hydrocarbon receptor, intranuclear hormone

receptor, estrogen receptor, androgen receptor and thyroid hormone receptor (claims 3-8). The claims are further drawn to such a cell wherein the transcription control region does not contain a sequence which would alter the transcription control activity as determined by the minimum promoter region and the LRTF recognition sequence (claim 17). The claims are further drawn to such a cell expressing an aryl hydrocarbon receptor and an Arnt receptor (claim 9), as well as methods for evaluating a chemical substance as an agonist or antagonist utilizing the above cells (claim 11-12). The claims are further drawn to a method for obtaining such a cell wherein the cell is an animal cell that comprises a DNA comprising a gene coding the LRTF which was introduced thereto before, after or during the same time as the reporter gene and marker gene are introduced into the cell (claims 14-15), and such a cell wherein the gene coding the LRTF comprises a selective marker gene different from gene (b) (claim 16).

Bradfield teaches the use of mammalian cells expressing the Ah receptor and the Arnt receptor in an assay to detect agonists of the transcriptional activities of the receptor (see column 23, lines 30-33 and lines 41-46). The detection assay concerns measuring the activity of a reporter gene that has been operatively linked to a transcriptional response element for the

Ah receptor (see column 2, lines 56-62). The Ah receptor is maintained in the cell on a plasmid also containing a selectable maker, while the reporter gene is presnt on a second plasmid, but in the same molecule with a second selectable marker (see Figure 11). Reporter gene (c) is not present in the cell containing the Ah receptor, reporter and selectable marker genes as described by Bradfield.

Bradfield does not teach such cells wherein the reporter gene (a) and the selective marker gene (b) have been stably transformed.

Waldman teaches a method for stable transfection of mammalian cells with DNA (see entire document, especially the abstract), wherein the DNA is maintained within the cells for more than 20 generations of growth. Waldman further teaches that the method is "fast, economical and of general utility" (see abstract, last sentence). Waldman further teaches that in the course of molecular biological work, "it is often desirable or necessary to develop cell lines containing one or very few copies of a particular DNA construct stably integrated into the genome" (page 216, 2nd column) and that the method of stable transfection taught in the reference "requires very little time, effort or expense to perform" (see page 221, second column, last paragraph).

It would have been obvious for one of ordinary skill in the art to combine the teachings of Waldman and Bradfield because both Waldman and Bradfield teach methods which involve the transfection of mammalian cells.

One of ordinary skill in the art would have been motivated to combine the teachings of Bradfield and Waldman because Waldman teaches that his method is "fast, economical and of general utility." One of ordinary skill in the art would also have been motivated to combine the teachings of Bradfield and Waldman because Waldman further teaches that his method "requires very little time, effort or expense to perform."

Based upon the teachings of the prior art, and based upon the high level of skill of one of ordinary skill in the art, there would have had a reasonable expectation of success when combining the teachings of Waldman and Bradfield.

Claims 1-9, 11-12 and 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bradfield et al (US Patent No. 5,650,283, of record; henceforth Bradfield) in view of Waldman and Waldman (Analytical Biochemistry 258:216-222, 1998, of record; henceforth Waldman) and further in view of Kushner et al (US Patent 6,117,638; henceforth Kushner).

This rejection is maintained for reasons of record.

Bradfield in view of Waldman teaches the invention as decribed above, but does not teach the following elements: the use of a TATA box as the minimum promoter (claim 2) or the identification of an antagonist for the LRTF (claim 12).

Kushner teaches a method for screening compounds in cells (including mammalian cells) that both activate (agonist function) and block (antagonist function) the stimulation of transcription of genes, some of which are regulated by hormone receptors, using a minimum promoter region comprised of a TATA box (see especially column 14, lines 39-49 and 57-64; and column 15, lines 32-41 and 60-63). Kushner further teaches that his method could be used to identify compounds which could attenuate the effects of hormone receptor transcription response hyperactivation, which is prevalent with respect to the estrogen receptor and its role in breast cancer formation (see Kushner column 15, lines 40-41).

It would have been obvious for one of ordinary skill in the art to combine the teachings of Bradfield in view of Waldman with the teachings of Kushner because both sets of references teach methods for determining the effects of a compound on the transcription of hormone responsive genes in mammalian cells.

One of ordinary skill would have been motivated to combine the teachings of Bradfield in view of Waldman with those of

Kushner to identify compounds which could attenuate (antagonize) the effects of hormone receptor transcription response hyperactivation which is prevalent with respect to the estrogen receptor and its role in breast cancer formation as taught by Kushner.

Based upon the teachings of the prior art and absent evidence to the contrary, one or ordinary skill in the art would have had a reasonable expectation of success when combining the references of Bradfield in view of Waldman with the teachings of Kushner.

Claims 1, 3-9, 11, 14-17 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bradfield et al (US Patent No. 5,650,283, of record; henceforth Bradfield) in view of Waldman and Waldman (Analytical Biochemistry 258:216-222, 1998, of record; henceforth Waldman) and further in view of O'Malley et al (US Patent 5,834,213; henceforth O'Malley).

Bradfield in view of Waldman teaches the invention as decribed above, but does not teach the use of an ovalbumin or metallothionein minimum promoter (claim 19).

O'Malley teaches a method for screening compounds in cells (including mammalian cells) that regulate transcription of genes, some of which are regulated by hormone receptors, using a

minimum promoter region which consists of a TATA element capable of binding RNA polymerase II and is selected from any of the commonly used elements such as the ovalbumin promoter (see entire document, especially column 5, lines 22-26). O'Malley further teaches that his method can be used to identify compounds which could regulate the effects of hormone receptor transcription responses from, for example, the estrogen and androgen receptors (column 5, lines 45-50). O'Malley further teaches that a hormone responsive element can be used in conjunction with, e.g., a thymidine kinase minimum promoter to monitor changes in expression of a reporter gene (column 7, Example 1). O'Malley also teaches that steroid hormones are potent modulators of transcriptional events and that they are further associated with differentiation, homeostasis and development (column 1, lines 24-26). O'Malley further teaches that his methods are useful for studying transcriptional responses and to identify compounds which regulate biological activity of hormone receptors as well as for allowing for rapid screening of a large number of compounds for their ability to regulate transcription responses (column 11, lines 16-31).

It would have been obvious for one of ordinary skill in the art to combine the teachings of Bradfield in view of Waldman with the teachings of O'Malley because both sets of references

teach methods for determining the effects of a compound on the transcription of hormone responsive genes in mammalian cells.

One of ordinary skill would have been motivated to combine the teachings of Bradfield in view of Waldman with those of O'Malley to rapidly identify large numbers of compounds which could regulate hormone receptor transcription, as taught by O'Malley.

Based upon the teachings of the prior art and absent evidence to the contrary, one or ordinary skill in the art would have had a reasonable expectation of success when combining the references of Bradfield in view of Waldman with the teachings of O'Malley.

Response to Arguments

Applicant argues that the reporter gene (a) of the instant claims is connected downstream from a transcription control region which substantially consists of a recognition sequence of the ligand-responsive transcription control factor and a minimum promoter, and that, as such, the constitutive background transcription activity is lowered. Applicant further argues that the lower background activity allows for higher sensitivity in the detection of ligand-responsive transcription activity. Applicant further argues that the prior-cited reference, whether

alone or in combination, fail to suggest or disclose the presently claimed subject matter, and that the references fail to recognize the fact that the present animal cell exhibits higher sensitivity in the detection of ligand-responsive transcription activity. Applicant further argues that the cited art fails to suggest or disclose a DNA comprising in a molecule, a reporter gene (a) connected downstream from a transcription control region which substantially consists of a recognition sequence of the ligand-responsive transcription control factor and a minimum promoter, and a selective marker gene (b) and that based upon this deficiency alone, the Office has failed to present a valid *prima facie* case of obviousness.

Applicant's arguments have been carefully considered and have been respectfully found unpersuasive for the following reasons. Applicant's assertion that the lower background activity with regard to transcription regulated by the transcription control region of the instant invention and Applicant's further assertion that the lower background activity allows for higher sensitivity in the detection of ligand-responsive transcription activity is not relevant because no recitation of such assertions are present in the instant claims. The combined references do indeed disclose a DNA comprising in a molecule a reporter gene (a) connected downstream from a

transcription control region which substantially consists of a recognition sequence of the ligand-responsive transcription control factor and a minimum promoter, and a selective marker gene (b) as presented in the above rejections. In fact, more than one example of prior art teaching such a cell comprising the recited DNA has been provided.

Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to the Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is (571) 273-8300. Note: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Walter Schlapkohl whose telephone number is (571) 272-4439. The examiner can normally be reached on Monday through Thursday from 8:30 AM to 6:00 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached at (571) 272-0781.

Walter A. Schlapkohl, Ph.D.
Patent Examiner
Art Unit 1636

March 29, 2006

NANCY VOGEL
PRIMARY EXAMINER